A Dissertation

On

A STUDY ON PULMONARY TUBERCULOSIS IN HIV REACTIVE PERSONS

GOVERNMENT MOHAN KUMARAMANGALAM MEDICAL COLLEGE

MD GENERAL MEDICINE

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

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CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON PULMONARY TUBERCULOSIS IN HIV REACTIVE PERSONS"** is a original work done by **Dr.K.THIYAGARAJAN** in **Government Mohan Kumaramangalam Medical College Hospital, Salem** to be submitted to **The Tamilnadu Dr.M.G.R.Medical university** in partial fulfillment of the university Rules and Regulations for the award of M.D – Degree Branch – I General medicine Under our supervision and guidance during the Academic Period from Oct 2003 to September 2006.

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CONTENTS

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INTRODUCTION

Tuberculosis, an ancient disease, continues to remain even today as a major public health problem in much of the developing countries like India.

The Problem is now complicated by relentless spread of Human Immunodeficiency virus (HIV) which causes Acquired Immunodeficiency syndrome (AIDS) pandemic and the emergence of multi drug resistant strains.

Infection with HIV results in progressive immunodeficiency and renders the infected person become increasingly vulnerable to wide range of pathogens. In many parts of the world Tuberculosis is the most common opportunistic infection in HIV infected person. The immune defects produced by HIV influence the natural course of TB infection.

Thus the HIV pandemic has altered both the epidemiology of TB and measures for approaches to its control. In populations where the risk of TB and HIV infections are high, the incidence of TB is expected to increase particularly in countries like India.

In this study, an attempt has been made to study the Clinical Spectrum, laboratory and radiological changes in patients having pulmonary TB in HIV Patients.

AIMS OF THE STUDY

1. To study the clinical spectrum of pulmonary TB and HIV patients attending our Medical college Hospital. (both inpatients and outpatients).

2. To study the laboratory and radiological changes in the above said patients.

3. To evaluate the diagnostic limitations of tuberculin test and sputum smear microscopy for AFB in patients having tuberculosis infection in HIV.

HISTORY

HISTORY OF TUBERCULOSIS

Evidence of TB has been found in the bones of prehistoric man in Germany, dating back to 2000 B.C. Also typical TB changes have been found in spines of skeleton of ancient Egyptian. (2500 to 1000 B.C)

Hippocrates also devoted some attention to this. Aristotle conceived the theory that TB is an infectious diseases. Villerriun in 1865 showed in a series of classical experiments that TB is caused by a specific agent that can be transmitted from man to animals by inoculation of infected material. Robert koch applied himself and in 1882 the elusive microbe was identified.

The discoveries of stethoscope by Laennec in 1819, and the works of Rudolph virchow the founder of the Cellular pathology, X ray, by Roentgen in 1895, allergy coined by Von Priquet in 1907 and BCG by Calmette and Guerin (from 1908 to 1921) evolutioned the study of TB in Humans.

HISTORY OF HIV

AIDS was first recognized in USA in 1981 by CDC.

In 1983 HIV Virus was isolated from a patient with lymphadenopathy and by 1984, it was demonstrated clearly to be the causative agent of AIDS. In 1985 sensitive ELISA was developed to diagnose it.

In India HIV was first identified from a commercial sex worker in chennai in 1986.

Early in the course of Human immunodeficiency syndrome, the link between HIV and TB was not clearly recognized. During the past decade TB has became the major opportunistic infection complicating the HIV epidemic worldwide.

By the year 2000, the prevalence of HIV and TB continued to climb worldwide. In 2000, the Global programme on AIDS of the WHO estimated the prevalence of HIV infection among adults and children worldwide was 36.1 million. At the same time about 2 billion people had latent infection with M.Tuberculosis and approximately 11.8 million people were co – infected.

REVIEW OF LITERATURE

EPIDEMIOLOGY

Mycobacterium Tuberculosis infects one third of the worlds population (i.e) about 1.9 billion people. Worldwide each year there are 8 million new cases of Tuberculosis with 3 million deaths.

This death comprise 25% of all available deaths in developing countries. 95% of TB cases and 98% of Tuberculosis deaths occur in developing countries. Three fourth of the TB cases in developing countries occur among the economically productive age group.(i.e) 15 to 50 years of age. Rate of TB infection are highest where people are poor and over crowded. Much of the TB burden is in South East Asia.

According to WHO 39% of all notified cases globally are contributed by countries of South East Asia followed by Western Pacific (25%), Africa (15%), Eastern Mediterranean (4%), Americas (7%), and European Regions (10%).

In South East Asia 95% of TB cases are reported from India, Indonesia, Myanmar, Thailand while in western Pacific great majority are from China, Philippines, Vietnam, Cambodia.

The situation is likely to be further complicated by the rapidly spreading HIV pandemic. Of the five million adults with HIV infection in South East Asia region, 1.5 million are likely to be infected with TB. Given the annual risk of clinical Tuberculosis which varies from 5 to 8% among dually infected individuals, further increase is Tuberculosis incidence seem inevitable.

Rapid increase in Tuberculosis attributed primarily to HIV have already been noticed in USA as well as in countries of sub – saharan Africa.

The dual epidemic of TB and HIV is also a significant problem in the developed countries. For the first time since 1953, an increase of 2.5% in TB cases was reported from USA in 1986.

The incidence of TB in HIV infected patient is about a hundred fold than that in the general population. Even more dramatic is the effect seen when person who are already infected with HIV became newly infected with Mycobacterium Tuberculosis.

In two outbreaks in which HIV infected persons were exposed to cases of infectious Tuberculosis, 40% of infected persons developed active TB within a few months. In HIV infected persons active TB seems to develop soon after infection and progresses rapidly, often resulting in death.

IMMUNOPATHOGENESIS OF TB IN HIV

The impact of HIV and TB infection is bidirectional (i.e) TB affects the natural history of HIV infection and HIV affects the presentation and natural history of TB. Substantial evidence exist that the consequence of HIV and TB infection are greater than would be the case for either condition singly.

A study from several Hospitals in USA examined the survival in a cohort of HIV infected patients who had been successfully treated for TB and compared the survival to a cohort of HIV infected person who had never had TB but were matched for $CD4^+$ counts. At every level of $CD4^+$ count survival in a Kaplan – Meier life table analysis was worse for patients who had TB than those who had not TB[17]. From this study TB accelerates the natural history of HIV infections and leads to earlier death.

Another study examined to the impact of concomitant TB in the course of HIV infection by comparing the HIV +ve patients with TB and without TB matched by CD4 counts. In this study TB was not an independent predictor of increased mortality but was associated with an increased risk of development opportunistic infections[18].

More direct evidence of accelerated HIV progression from TB is provided by several invitro studies examining the interaction between the M.Tuberculosis and HIV at the molecular level. Zhang et al[19]. demonstrated that both cell wall components and whole M.Tuberculosis organisms increased the transcription of the long terminal repeat (LTR) of HIV invitro. This seems to be mediated through the activation of transcription factors nuclear factor KB (NF-KB) and IL – 6 The same investigator demonstrator this invivo by comparing HIV viral copies taken from bronchial alveolar lavage (BAL) samples from radiographically abnormal areas of lungs of TB patients with those from normal segments and with samples taken from patients without TB.

Branched DNA levels of HIV were highest in samples taken from radiographically abnormal segments of lungs in HIV positive TB patients compared with controls. In addition branched DNA levels of HIV declined over time with TB treatment[20].

IMPACT OF HIV ON TB.

$CD4^+$ T lymphocytes and macrophages have a central role in the immune response to mycobacterial infections. HIV infections results in progressive depletion and dysfunction in $CD4^+$ cells with defect in macrophages and monocyte function[21].

As a result of this, HIV infected patients have an increased risk of reactivation of latent TB as well as increased risk of disease from new infection.[6,22,23.] In a prospective longitudinal study Guelar et al[22] found a mean $CD4^+$count of 77$\pm$ 103 cells / mm^3 (range 1 to 400 cells / mm^3) in 23 of 733 HIV infected PPD negative who ultimately developed TB. The mean $CD4^+$of this above entire groups was 377 $\pm$ 260 cells / mm^3.

Macrophages based resistance against TB is due to its ability to control intracellular mycobacterial growth. $CD4^+$ lymphocytes prime macrophages to control intracellular growth by releasing cytokines such as IF - γ, IL-1, IL-2 and TNF -α which activate blood born macrophages. An additional protective mechanism may be the generation of cytolytic T cells in response to mycobacteria[24]. $CD4^+$ T cells and γ/δ T cells kill autologous infected macrophages[25, 26].

Forte et al[27] demonstrated decreased cytolytic T cell activity in HIV infected patients. The continued loss of $CD4^+$ cells in HIV seropositive patients and their reduced production of IL-2 may be the causes of decreased cytolytic T cell activity[28] .

While the $CD4^+$ cell decline over progressive HIV infection, the number of $CD8^+$ cells and γ/δ T cell often increase[29]. Their role in the development of TB in HIV infected patients remains to be defined.

IMPACT OF TB ON HIV

TB can accelerate the course of HIV infection[17,30,31] Toosi et al[32] demonstrated enhanced susceptibility of blood monocytes from patients with TB to produce infection with HIV-1. As noted previously, infection with M.Tuberculosis stimulates release of mononuclear cytokines such as IL-1, IL-2, IL-6 and TNF-α. M.Tuberculosis upregulates genes for these cytokines[33].

These cytokines enhance replication of HIV-1 invitro using several lines[34] the mechanism of this stimulation has been localized to the 5'LTR of HIV–1; more specifically to the NF-KB transcription enhancer site[35]. Recently Zhang et al[19] demonstrated that M.Tuberculosis and its major antigenic cell wall component Lipoarobinomannan were potent inducers of HIV-1 replication and LTR transcription via nuclear factor NF-KB and IL–6 sites. This was through direct and indirect stimulation by the cytokines IL –1 and TNF-α. These data suggest that the cytokines involve in the defense against TB may be deleterious in HIV seropositive patients. The interaction between HIV and TB may increase viral burden accelerating progression to advanced stage of HIV disease[36].

There is also a major impact of HIV infection on the natural history of TB. The major defect in immune function in patients with HIV infection is related mainly though not entirely to the decline in numbers and impairment of function of

$CD4^+$ T cells. These now substantial evidence from studies in human that $CD4^+$ T Cell are of crucial importance in initiating and maintaining an effective host immune response against TB.

$CD4^+$ T cells are classified in to atleast two types namely TH^1 and TH^2 cells. TH^1 and TH^2 had different phenotypes based on the patterns of cytokines which they secrete[37]. TH^1 cells primarily secrete IFN-γ whereas TH^2 cells secrete IL-4, IL-5 and IL-10. It had been previously shown that a TH^1 type response represented a favourable immune response in patients with Leprosy as compared TH^2 response in the same disease.

Yamamura et al[38] took biopsy specimens from Tuberculoid Leprosy lesions (Paucibacillary lesions without a great deal of tissue necrosis) and compared cytokines gene expression patterns with those seen in specimens from Lepromatous leprosy lesion (multibacillary lesion with extensive tissue necrosis).

In the tuberculoid lesions the inflammatory infiltrate consists of T lymphocytes with high levels of mRNA transcription for IFN - γ, IL-1. By contrast, in lepromatous lesions, the infiltrate is characterized by T cells with high levels of m RNA transcripts for IL–4, IL-5, and IL–10. These findings suggested that a TH^1 type response is beneficial in response to infectious diseases.

Direct evidence of the beneficial nature of a TH^1 type response in TB comes from studies by Condos et al[39] who examined local immune responses in the lungs of patients with active pulmonary-TB. In patients with radiographically and clinically minimal diseases (i.e Noncavitory infiltrates and sputum samples that were negative for AFB on smear), there was a lymphocytic alveolitis characterized by cells that produced locally high amounts of IFN-γ. In contrast, patients with advanced cavitory smear positive TB did not produce high levels of IFN - γ.

The significance of IFN - γ was further demonstrated by the same groups of investigators, who showed that exogenously administered IFN - γ had beneficial effects in patients with MDR TB[40]. These clinical studies support a large number of invitro and animal studies that also demonstrate an important role for IFN - γ is host defense against TB. These studies have established that this proinflammatory cytokine has several effects at the cellular level that are important in host defense against intracellular pathogens. This includes activation of alveolar macrophages leading to the production of reactive oxygen and nitrogen species considered important in growth inhibition and killing of M.Tuberculosis, increased expression of major HLA Complex class II and increased migration of lymphocytes.

As $CD4^+$ cells are the major source of IFN γ and $CD4^+$ cell count and function are depressed in patients with HIV infection, it stands to reason from the foregoing discussion that HIV infected persons would be especially susceptible to TB infection and disease.

TUBERCULIN SKIN REACTIVITY

Tuberculin skin reactivity is dependent on lymphokines release. The Tuberculin skin test is a delayed type hypersensitivity reaction that generally parallels cellular immunity.

Anergy, which develops as a consequence of progressive HIV infection undermines effort to detect occult TB infection in those who are greatest risk for active disease. Johnson et al[41] demonstrated that among patients with active TB, approximately 30% of those who were HIV seropositive and more than 60% of those with AIDS had tuberculin skin reaction to 5-Tu comprising less than 10mm of induration.

Similarly Heubner et al[42] found that anergy was four times and 15 times as likely for persons with $CD4^+$ counts of 200 to 400 cells / mm^3 and less than 200 cells / mm^3 respectively as for persons with more than 499 $CD4^+$ cells / mm^3.

However 40% of patients with counts less than 200 cells/mm^3 were not anergic, suggesting that a CD4 cut off for assuming anergy could be misleading.

Because of increased anergy, reactions of 5 mm of induration or larger are considered positive.

Graham et al[43] showed that skin test positivity varied markedly between HIV positive (14%) and HIV negative (25%) patients, suggesting a cut off definition of 2mm of induration or more in HIV positive patients.

In contrast Heubner et al[44] found that small (1 to 4mm) tuberculin skin test reaction in HIV infected patients did not represent diminished reactivity due to HIV. They concluded that individuals who react to other delayed type hypersensitivity antigen should also mount a significant reaction ($\geqq$ 5mm) to tuberculin if they are truly infected with M.Tuberculosis. Any test in a HIV positive persons with a reaction of 5mm or greater should be considered positive.

CLINICAL PRESENTATION

Pulmonary involvement occurs in atleast 75% of all HIV infected patients with TB. Symptoms and physical findings are usually not predictive of TB in HIV seropositive patients.

Unfortunately fever, sweats, fatigue, weight loss, anorexia and cough are very common symptoms in HIV seropositive patients and are suggestive of diseases such as Pneumocystis pneumonia, Histoplasmosis, Lymphoma wasting syndrome and MAC infection.

M.Tuberculosis is now regarded as the most common cause of fever of unknown origin in HIV infected patients. Modilevsky et al[50] found fever (91%) and cough (84%) to be the most common presenting symptom in a retropective study of 39 patients in Los Angeles. Other symptoms included a mean weight loss of 11$\pm$ 3.2kg, dyspnoea (64%), chest pain (25%), as well as extra pulmonary symptoms such as diorrhoea (54%) and abdominal pain (26%). On physical examination the mean temperature was 39.2 $\pm$ 0.8^0C and tachypnea was observed in only 36% of patients.

In a study by Soumya Swaminathan et al[3] the distribution of symptoms were cough (97%), weight loss (94%), fever (79%), dyspnea (68%), chest pain (47%), and hemoptysis (18%). The distribution of clinical signs were muscle wasting (47%), Oral thrush (38%), Lymphadenopathy (29%), Clubbing (18%), Pedal oedema (9%), Bronchial breathing (14%), Rhonchi (14%), Crepitations (55%).

In Tambaram study[2] the symptoms were Cough (85.43%), Fever (63.06), Dyspnoea (61.31%), Odynophagia (60.44%), Anorexia (51.44%), Weight loss (49.69%), Diarrhoea (33.81%), Chest Pain (19.81%), Fever with rigor (18.00%), Haemoptysis (11.50%). The physical signs were Tamabaram Tongue (87.93%), Nail changes (52.63%), Clubbing (46.00%), Respiratory distress (42.94), Oral thrush (40.81%), Wasting (36.13%), Jaundice (18.81%), Genital ulcers (18.50%), Skin lesions (17.13%), CNS manifestations (13.63%) and Herpes Zoster (11.81%).

Because signs and symptoms are so non-specific, tuberculin skin testing could be a useful part of the clinical evaluation. However more than 50% of patients with active TB and another AIDS defining diagnosis are anergic[8,9,41] . Negative PPD results and anergy were more common with increasing immunodeficiency as measured by $CD4^+$ counts.

Markers of severity such as mycobacterimia and positive AFB smears were more common in patients with markedly depressed $CD4^+$ cells counts, according to Jones et al[49].

In contrast tuberculous pleuritis and positive tuberculin skin test results, which are dependent on the integrity of cellular immunity were more common in patients with higher $CD4^+$ cell counts. In most industrialized countries, the clinical features of TB vary according to the degree of immunosuppression and atypical

presentation are more commonly found among the immunosuppressed patients. This may not be true for extrapulmonary TB[5].

In sub-Saharan Africa, patients with HIV related TB are more likely to present with extrapulmonary disease, miliary infiltrates, and non reactive tuberculin test responses than are those without HIV infection[11-14,15,16,51] . African studies have provided clinical correlation with $CD4^+$ cell counts. Whether patients who have been reported in African series were more immunosuppressed is unknown.

RADIOLOGICAL FINDINGS

The spectrum of radiological findings of TB in HIV infected patients is similar to that observed in seronagative patients. A compilation of reported radiologic findings from 15 studies involving 457 HIV positive patients in USA revealed that more than 30% patients presented with hilar or mediastinal adenopathy[6,8-10,45-49,52-55]. Cavitation was present in only 18% of patients, while apical or upper lobe infiltrates were seen in slightly more than 25%. Lower lobe infiltrates (10%), diffuse or miliary patterns (7%) and pleural effusions (17%) were also observed. Normal appearing chest radiographs were found in 6% of patients with proved TB. However these tactics are misleading. As with clinical findings

radiographic manifestations appear to correlate with the degree of immunosuppression.

In Tambaram study[2] the radiological patterns of pulmonary tuberculosis in seropositive TB patients are as follows.

Upper zones	-	Exudative	-	34.80%
		Nodular	-	23.69%
		Fibrotic	-	21.98%
		Cavities	-	17.21%
Mid & lower zones	-	Exudative	-	41.58%
		Nodular	-	26.53%
		Fibrotic	-	7.60%
		Cavities	-	7.08%
All zones	-	Miliary	-	5.14%

In a study by Soumya Swaminathan et al[3] the Radiological lesions at presentation were Normal X-ray - 9%, Pleural effusion - 12%, Mediastinal glands - 3%, Pneumothorax - 2%, Opacities in Focal U/L, Focal L/L, Extensive were 9%,14%, and 38% respectively. Cavation U/L - 11%, L/L - 3% and Miliary tuberculosis - 17% were also reported.

Greenberg et al[52] , correlated radiographic findings with $CD4^+$ cell counts in 68 patients. 55% of patients with $CD4^+$ cell counts greater than 200/mm^3 showed a typical post primary pattern compared with only 23% of those with $CD4^+$ cell counts with less than 200 /mm^3.

Jones et al[49] found mediastinal adeopathy in 21of 58 patients [30% with fewer than 200 $CD4^+$ cell / mm^3 compared with only four (13%)of patients with more than 200 $CD4^+$ cell / mm^3]. In contrast pleural effusion were present in 6 of 58 (10%) patients with $CD4^+$ cell less than 200 /mm^3 verses 8 (27%) of 30 patients with more than 200 cells / mm^3.

Thus HIV seropositive patients with less immunosuppression (i.e higher $CD4^+$ cell counts) often have radiographic findings typical for reactivation. These include infiltrates in the posterior segment of upper lobes and superior segment of lower lobes. Cavitation may be present.

As immunosuppression increases with falling $CD4^+$ cell counts, "atypical" findings occur more frequently. Infiltrates can be focal, occurring in the middle and lower lobes more frequently or can be diffuse, reticular, nodular or even miliary. Upper lobe infiltrates and cavitation are unusual. Chest radiography may also appear normal in 7% to 14% of patients[52,56] . The clinician must maintain a

high index of suspicion for TB in a patient who present with cough and sputum production but a normal appearing chest radiograph[57].

Unilateral and bilateral pleural effusion occur with varying frequency ranging from 10% to 38 % [8-10,46,48,49,52,56,58]. In a series from USA 44 to 50% had associated infiltrates and 5% to 20% presented with hilar and or mediastinal adenopathy. Effusions were bilateral in 10% to 28% of patients[59,60]. Similarly Batungwanayo et al[61], in a study of HIV related Tuberculous effusions in Kigali, Rwanda found associated localized infiltrates (28%), miliary patterns (14%) and adenopathy (11%) in 57 patients with AIDS.

Richter et al[62] , in a prospective study of HIV seropositive patients with tuberculous effusions in Dar es Salaam, Tanzania reported that one third of the patients had evidence of disseminated tuberculosis disease.

Radionucleotide studies are not routinely performed in patients with TB. However in the workup of AIDS patients presenting with pulmonary complications, Gallium scans have proved useful in distinguishing different manifestations[63]. TB and lymphoma commonly show focal uptake in the hilar, mediastinal and lung parenchyma.Thallium shows high affinity for certain tumours such as Kaposi sarcoma and lymphoma.

Lee et al[64] have demonstrated that sequential thallium – gallium scans display a focal mismatch that is specific for mycobacterial infections though fungal disease due to Cryptococcosis, Histoplasmosis and Coccidiodomycosis cannot be excluded.

The role of CT of the chest is limited because findings are usually nonspecific. However subtle abnormalities like miliary pattern or unusual cavitation may be found and highly characteristic finding is the presence of low density hilar and mediastianal nodes. Peripheral enhancement of enlarged nodes is observed following the intravenous administration of contrast material. The low density areas located centrally within the nodes are presumably due to caseation or liquefaction necrosis.

DIAGNOSIS

SPUTUM FOR ACID FAST BACILLI

It is estimated that sputum AFB smears are positive in 65% to 75% of HIV seronegative patients who have had multiple specimens and in 30% to 40% of those with a single specimen[66-68]. In a non HIV setting Kim et al[66] found positive smears in 20% to 40% of patients with minimal diseases, in 60% to 70% of patients with moderate disease and 90% to 95% of patients with advanced cavitary

disease. Similarly Greenbaum et al reported[68] positive smears in 52% of patients with cavitary disease but in only 32% of patients with local infiltrates.

Barnes et al[69] found positive smears in 90% of patients with radiographic findings typical of adult reactivation and for 98% of patients with cavitary TB, AFB was found on sputum smear.

In a study by Soumya Swaminathan et al[3], of the 65 cases who had culture confirmed pulmonary tuberculosis, 83% were smear positive at intake. In Tambaram study[2], of the total 1600 having tuberculosis and HIV disease, just 235 patients (15%) were sputum positive.

SPUTUM CULTURE

It remains the gold – standard for diagnosis of pulmonary Tuberculosis. In resource poor countries, the diagnosis is heavily dependent on the sputum AFB smears.

HIV positive patients have been reported to have a lower yield in AFB smears. Brindle et al[70], measured the concentration of viable tubercle bacilli in sputum. HIV patients excreted slightly fewer organisms per ml of sputum than did HIV negative patients with culture confirmed Tuberculosis. Positive AFB smears

were observed in 31% to 89% of patients; culture were positive in 85% to 100% of patients.

Kleen et al[71], found that only 11 of 38 patients (29%) with AIDS or AIDS related complex had an initial positive smear compared with 35 of 57 control patients (61%).

Repeated sputum samples (up to 5) brought the yield to 45%. In a study by Kramer et al[7] analyising the reasons for delayed diagnosis of TB, the most frequent problem was that too few (fewer than 3) sputum samples were obtained for mycobacterial study in patients with respiratory symptoms and radiographic findings suggestive of TB.

The sensitivity of sputum smears may be greater in patients with less immunosuppression because they present with X-ray picture typical of reactivation. Close to 90% of patients with pulmonary TB have an abnormal chest radiographs where as up to 10% have a normal chest radiograph. Findings of classic TB such as apical infiltrates and cavitation are less common in HIV infected patients; and lower lung disease is more common as are lymphadenopathy, pleural effusions and interstitial infiltrates.

FIBROOPTTIC BRONCHOSCOPY

It is a useful means of making a rapid diagnosis of TB in selective patients. Miro et al[72] studied 27 high risk patients for HIV infections. Positive AFB smears were found in the sputum, BAL fluid and / or bronchial washings in 30% of patients, compared with a 37% positive yield form bronchial brushings and /or transbronchial biopsy specimens (p value not significant). The addition of the transbronchial biopsy specimen increased the culture yield from 96% to 100% (p value not significant). They concluded that transbronchial biopsy did not contribute significantly to the diagnosis of TB.

In contrast, in a retrospective study, Kennedy et al[73] found that transbronchial biopsy provided the exclusive means for rapid diagnosis in 6 of 59 patients by demonstrating granuloma. BAL provided the diagnosis in 7 of 60 patients exclusively.

Transbronchial needle biopsy of mediastinal adenopathy has also proved useful for diagnosing TB in otherwise sputum negative and bronchoscopy negative patients[74]. When bronchoscopy is performed, the appropriate infection control practices for both HIV and TB must be followed.

POLYMERISE CHAIN REACTION

The diagnostic approach that has elicited most excitement recently is PCR. Diagnostic PCR is a DNA amplification technique that utilizes specific DNA sequences to serve as the marker for the presence of the organisms. Theoretically PCR may detect fewer than 10 organisms in a specimen in contrast to the 10,000 organisms per ml necessary for sputum AFB positivity.

In studies by Walker et al[75] and Schluger et al[76], they found that PCR has higher sensitivity but only lower specificity. It has sensitivity of 100% but specificity of only 70%.

Because of the limited clinical experience, as well as its cost and technical expertise, routine use of PCR cannot be recommended although this is unquestionably true that this technique represents its superiority over AFB smears in previously untreated TB patients[71].

Regarding the pleural specimens, only the percentages for AFB on pleural tissue and AFB cultures were statistically greater in HIV positive patients than HIV negative patients[59].

Although most common practice prior to AIDS epidemic, blood culturing for mycobacterial growth is routine in HIV infected patients, the frequency of positive blood cultures were inversely proportional to the $CD4^+$ cell counts. Jones et al[49] found that blood cultures were the only extra pulmonary source of M.Tuberculosis in 13 of 43 patients with no more than 100 $CD4^+$ cell counts.

EXTRA PULMONARY TUBERCULOSIS IN HIV PATIENTS

Since 1987 extrapulmonary TB has been has accepted as an AIDS defining diagnosis. The frequency may be related to the degree of immunosuppression as well as to the extend of diagnostic assessment[49,78]. The frequency of extrapulmonary TB ranged from 25% to 66%.

The common presentation are as disseminated TB (blood, bonemarrow or liver), TB of genitourinary tract, peripheral lymphnodes, pleura, central nervous system and abdomen including nodes in peritoneum and mediastinum.

Dissemination was categorized either as miliary TB (miliary pattern on X-ray, or miliary lesion in liver, bonemarrow biopsy or autopsy) or focal disseminated (concurrent involvement of atleast 2 noncontiguous organ sites.)

Not all studies found a progressive increase in the frequency of extra pulmonary TB with decreasing $CD4^+$ cell counts. Certain studies like Llibre et al[79] indicates the above statement.

Certain studies like above one, cervical lymphadenopathy was the most common extrapulmonary site. Lymphadenopathy either intrathoracic or extrathoracic is the most common extrapulmonary manifestation.

In patients with extrapulmonary TB, normal appearing chest radiographs are found in 10 to 15% of patients, which is similar to non HIV patients.

Regarding the AFB in stool, it was found to be positive in about 40% of patients with TB in HIV[50]. This probably represents organisms in swallowed sputum, since these patients have positive sputum smears and rarely exhibit gastrointestinal TB.

An unusual extrapulmonary manifestation is the formation of TB abscess in atypical location, like in neck, mediastinum, liver, abdominal wall, pancreas, and psoas muscle.

MULTI DRUG RESISTANT TB IN HIV

HIV infected patients more likely to acquire TB when exposed to other patients with TB.

Recently several outbreaks of MDR-TB in HIV were reported, indicating the rapid emergence of MDR-TB in HIV.

Factors that have led to these MDR-TB outbreaks are multiple. They are as follows :

(i) Increased transmission of MDR-TB to other HIV patients.

(ii) Delay in the diagnosis and treatment of TB in HIV.

(iii) Failure to achieve full compliance because of poor physical condition of the patient especially in countries like India, Sub-Saharan African countries.

(iv) Failure to recognise drug resistance and many more.]

TREATMENT

Centres for disease control (CDC) advisory panel has revised recommendations for treatment of tuberculosis in HIV infected patients. Based on the substantial potential benefit of highly active, antiretroviral therapy (HAART) and availability of numerous drugs active against HIV, withholding antiretroviral therapy until completion of therapy for tuberculosis is no longer recommended.

The currently recommended regimens provided three options for treatment of Tuberculosis in HIV infected patients. The guiding principles of these options are

(i) that Antiretroviral therapy should be administered when indicated,

(ii) that a short course regimen (treatment course of 6 to 9 months depending on the regimen), administered as directly observed therapy is preferred in treatment of tuberculosis because of improved compliance and

(iii) Because of its more favourable drug interaction profile, Rifabutin is preferred over Rifampin.

Rifampin is contraindicated for use with Protease inhibitors and non-nucleoside reverse transcriptase inhibitas (eg. Nevirapine, Delaviridine) because it is a potent inducer of cytochrome P-450 enzyme system that metabolises these drugs and thereby decreases concentrations of these antiretroviral agents to sub therapeutic levels.

Rifabutin is a less potent inducer of cytochrome P-450 enzymes and therefore has less of an effect on Protease inhibitor concentrations. Rifabutin is also substrate for cytochrome P-450 enzymes which protease inhibitors inhibit leading to accumulation of Rifabutin to potentially toxic levels. This interaction however permits lowering the dose of Rifabutin, which in turn has less of an effect on protease inhibitors levels.

Drugs interaction between Rifabutin and Ritonavir, hard gel Saquinavir or Delaviridine are significant. Therefore use of any Rifamycins with these agent is contraindicated or not recommended.

Nucleoside reverse transcriptase inhibitors have no important interaction with Rifamycins and they may be used. Like wise, antituberculous medications other than the Rifamycins have no significant interaction with any nucleoside or non nucleoside reverse transcriptase inhibitors or protease inhibitors and may be used.

If a protease inhibitors or non nucleoside reverse transcriptase inhibitors is to be started after giving Rifampicin, then atleast 2 weeks should elapse after the last does of Rifampicins. This time gape is necessary for reduction the enzyme inducing activity of Rifampicins prior to commencement of ARV.

ATT FOR PATIENTS ON ARV

If a patients already on ART develops active TB, then the ART should be suitably modified to be compatible with RNTCP regimens. Treatment of TB patients co infected with HIV cannot be envisaged without Rifampin. In TB patients co infected with HIV, treatment should be first administered for TB under the DOTS regimens and if the patients clinical condition allow, ART should be

started after completion of TB treatment. In patients with very low $CD4^+$ cell count, requiring concomitant administration of ART and ATT, the ARV regimen should be modified by replacing Nevirapine with Efavirenz. On completion of TB treatment such patients can be switched back to Nevirapine.

Efavirenz is contraindicated in pregnant women due to its teratogenicity. Rifampicin reduces the drug exposure to Nevirapine and dose adjustment for Nevirapine co-administered with Rifampicin has not been established.

Options for treatment of TB in HIV infected patients who are receiving Antiretro viral therapy[1] are as follows :

OPTION – I

1. INH 300mg + RBT 150mg + PZA 25mg / kg + EMB 15mg / kg daily for 2 months.
2. Then INH + RBT daily at the same doses for 4 months or INH 900 mg + RBT 300mg twice weekly for 4 months.
3. Do not use Ritonovir, Hardgel saquinavir, or Delaviridine for Antiretroviral therapy.

OPTION – II

1. INH 300mg + PZA 25mg / kg + EMB 15mg / kg + SM 15mg / kg (1g) daily for 2 months then
2. INH 300mg + PZA 25mg / kg + SM 25 to 30mg / kg (1.5g) two to three times a week for 7 months.

OPTION – III[+]

1. INH 300mg + RIF 600mg + PZA 25mg /kg + EMB 15mg / kg daily for 2 months then
2. INH 300mg + RIF 600mg daily for 4 months or INH 900mg + RIF 600mg thrice weekly for 4 months.
3. This regimen should be reserved for patients who either are not receiving Antiretroviraltherapy or who are receiving Antiretroviraltherapy consisting only of Nucleoside reverse transcriptase inhibitors.

- The dose of Rifabutin is 300mg daily if the patients is not taking a protease inhibitor or a non – nucleoside reverse transcriptase inhibitors.

[+] - Alternatively INH + RIF + PZA + EMB may be administered as a thrice weekly regimen for 6 months.

In general, anti TB treatment is the same for HIV infected person as it is for others and all patients should be treated with RNTCP regimen under the DOTS strategy.

All new TB cases known to be HIV positive should be treated with category – I regimen since they are more likely to be seriously ill. The retreatment cases are to be treated with category – II regimen. RNTCP regimens if supervised properly are as effective in HIV positive patients as in HIV negative patients.

TB in patients who are infected by a strain that is resistant only to INH should be treated with < 3 drug regimen or RIF, PZA and EMB for the duration of the entire period either as daily dosing or thrice weekly regimen for 6 to 9 months; but for atleast 6 months after conversion of culture / smear to negative.

In cases of mono Rifampin resistant organism, they should receive INH, PZA, EMB and SM regimen (Option - II). Sputum culture and smear should be monitored monthly to document their conversion to negative.

CHEMO PROPHYLAXIS FOR TUBERCULOSIS

Preventive therapy for TB (i.e. treatment for latent TB infection) reduces the risk of development of active TB disease in HIV infected individuals, although the durability of this effect may be limited by high rates of re-infection with TB in high TB burden countries like India.

WHO recommends TB preventive therapy if possible in areas where diagnostic testing such as X-ray chest, is available to exclude active TB disease and where PPD skin testing is feasible. INH therapy for 6 months in PPD skin reactors could be given after exclusion of active TB disease.

In India, however INH prophylaxis is not recommended due to

(a) Difficulty in excluding active TB disease in those with HIV and TB co-infection.

(b) as the burden of TB is high in India, chemoprophylaxis may not be able to prevent the re-infection.

(c) widespread use of INH for chemoprophylaxis without a system to ensure adherence to treatment may contribute to further increase in INH resistance.

(d) PPD skin test may not be feasible and also not reliable in severely immunocompromised patients.

BCG AND HIV

WHO and UNICEF recommend that asymptomatic HIV infected children should receive BCG vaccination as per the immunisation policies, but should be withheld in a child having symptomatic HIV infection. BCG when given to a symptomatic HIV positive children will lead to disseminated BCG disease[4].

MATERIALS AND METHODS

The study was conducted in the Antiretroviral therapy (ART) op in Government Mohan Kumaramangalam Medical College Hospital, Salem in 2005.

INCLUSION CRITERIA

1. Patients included in the age group between 12 and 60.
2. Patients with $CD4^+$ cells counts with less than or equal to 200 cells per mm^3 ($\leq$ 200).
3. Newly diagnosed cases of pulmonary TB in HIV patients.
4. Both sputum positive and sputum negative with X-ray and clinical evidence of PTB in HIV positive patients.
5. Patients having pulmonary manifestations only.

EXCLUSION CRITERIA

1. Patients with age group of < 12 and > 60.
2. Patients with $CD4^+$ cell counts more than 200 cells per mm^3 (> 200).
3. Patients having only extrapulmonary manifestation like, pleural effusion, lymphadenopathy, Meningitis etc.
4. Patients having chronic ailements like CRF, Diabetes Mellitus, CCF, Stroke etc.

METHODS

In this study, the eligible patients attending both medicine OPD and ART OP were evaluated in the following way.

(a) Detailed History taking.

(b) Physical examination.

(c) Laboratory examinations which includes complete hemogram, blood biochemistry, Sputum smears, X – ray chest, $CD4^+$ cell count, Tuberculin test and LFT, if needed USG abdomen and CT scan.

The details are collected in a Proforma.

PROFORMA

NAME :	**AGE :**	**SEX :**	**OP/IP NO :**
F/H NAME :	**OCCUPATION :**		
INCOME :			
ADDRESS :			
SYMPTOMATOLOGY :			
COUGH			
SPUTUM	Quantity	Character	Smell
HEMOPTYSIS	Yes	No	
	No of episodes		
	Amount		
BREATHLESSNESS			
	Dyspnoea	Grade	
WHEEZE	Yes	No	
CHEST PAIN	Yes	No	
FEVER	Continuous	Intermittent	
	Evening Rise of Temperature		
APPETITE			
WEIGHT LOSS			
ASSOCIATED SYMPTOMS :		Skin Lesion (Recent)	
		Diarrhoea	

PAST HISTORY :

H/O OF STD EXPOSURE	Pre-Marital	Extra-Marital
	Homo	Hetero
	No of Exposures	
H/O OF BLOOD TRANSFUSION	Yes	No
	When	
H/O OF NEEDLE PRICK	Yes	No

H/O OF DIABETES MELLITUS

H/O OF HYPERTENSION

H/O OF BRANCHIAL ASTHMA

PERSONAL HISTORY

Alcoholism	Smoker	Any other

FAMILY HISTORY :

Spouse	Alive	Dead
		Cause
		When

SOCIAL HISTORY :

Occupation

TREATMENT HISTORY :

Drugs taken

GENERAL EXAMINATION :

Build : Nourishment :

Anemia Jaundice Cyanosis Clubbing Weight

LYMPH ADENOPATHY :

SKIN LESION :

GENITAL LESION :

RESPIRATORY SYSTEM :

INSPECTION :

PALPATION :

PERCUSSION :

AUSCULTATION :

CVS :

ABDOMEN :

CNS :

INVESTIGATIONS

BLOOD :

TC DC ESR HB%

URINE COMPLETE :

Alb Sugar Puscells

BLOOD SUGAR :

BLOOD UREA :

S.CREATININE :

S.ELECTROLYTES :

LFT :

SPUTUM : 1.

2.

3.

CXR PA VIEW

ECG :

USG ABDOMEN / CT THORAX

$CD4^+$ CELL COUNT :

ABSOLUTE LYMPHOCYTE COUNT :

RESULTS

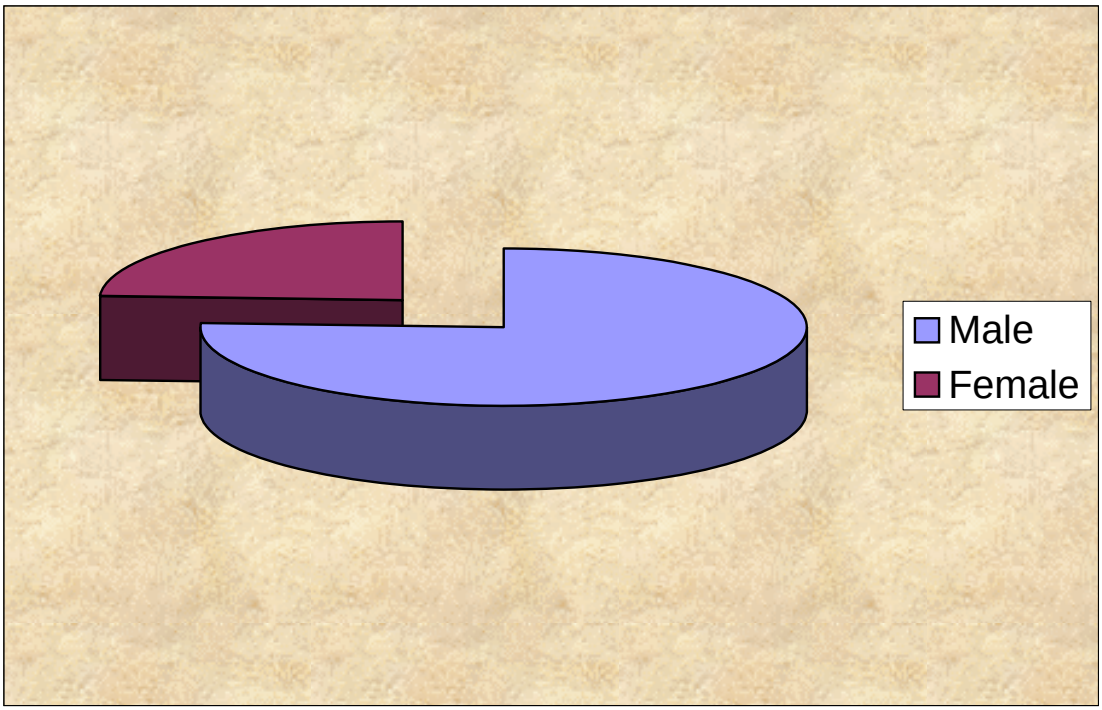
The study group included 70 patients with $CD4^+$ cell counts less than or equal to 200 cells per mm^3 ($\leq$ 200).

SEX DISTRIBUTION

In 70 patients sex distribution was

Table - 1

Male	**53**
Female	**17**



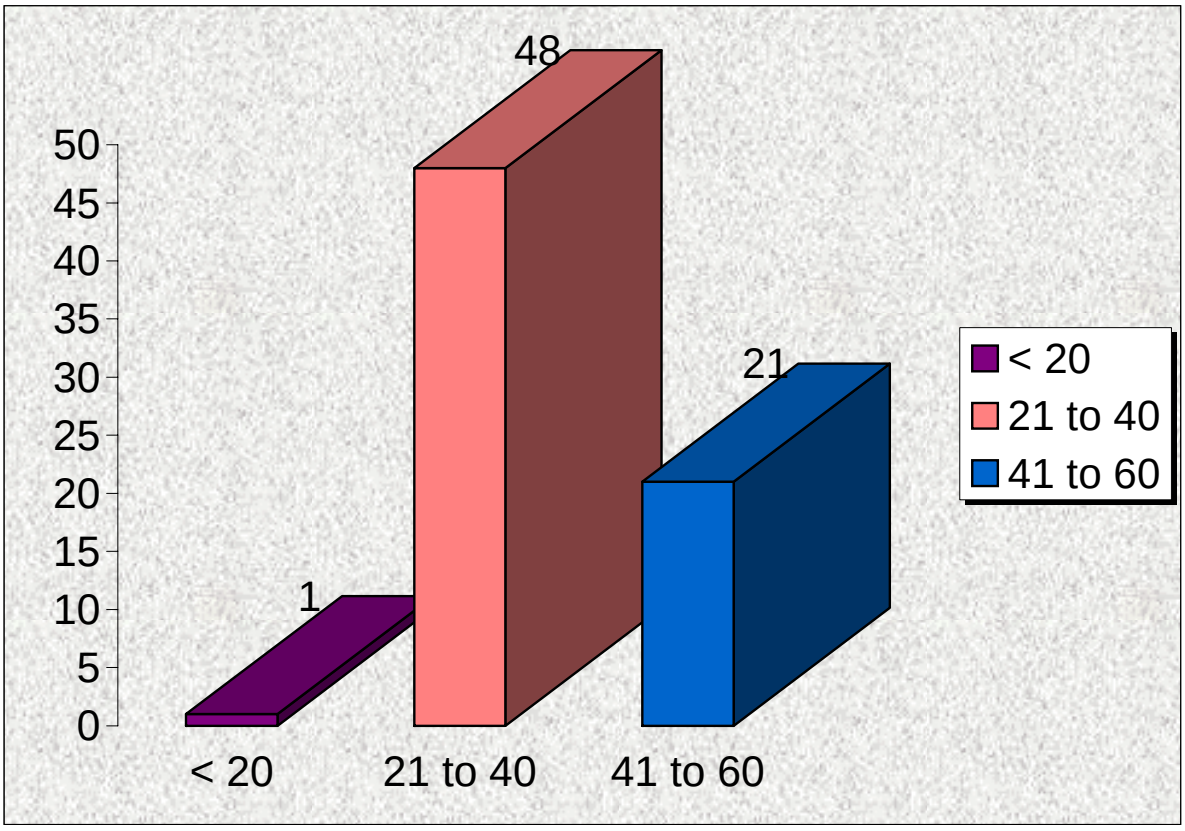
AGE DISTRIBUTIONS

The age distributions were

1. ≤ 20 – 1 patients
2. 21 to 40 – 48 patients
3. 41 to 60 – 21 patients

Table - 2

Age	No. of Patients
≤ 20	**1**
21 to 40	**48**
41 to 60	**21**

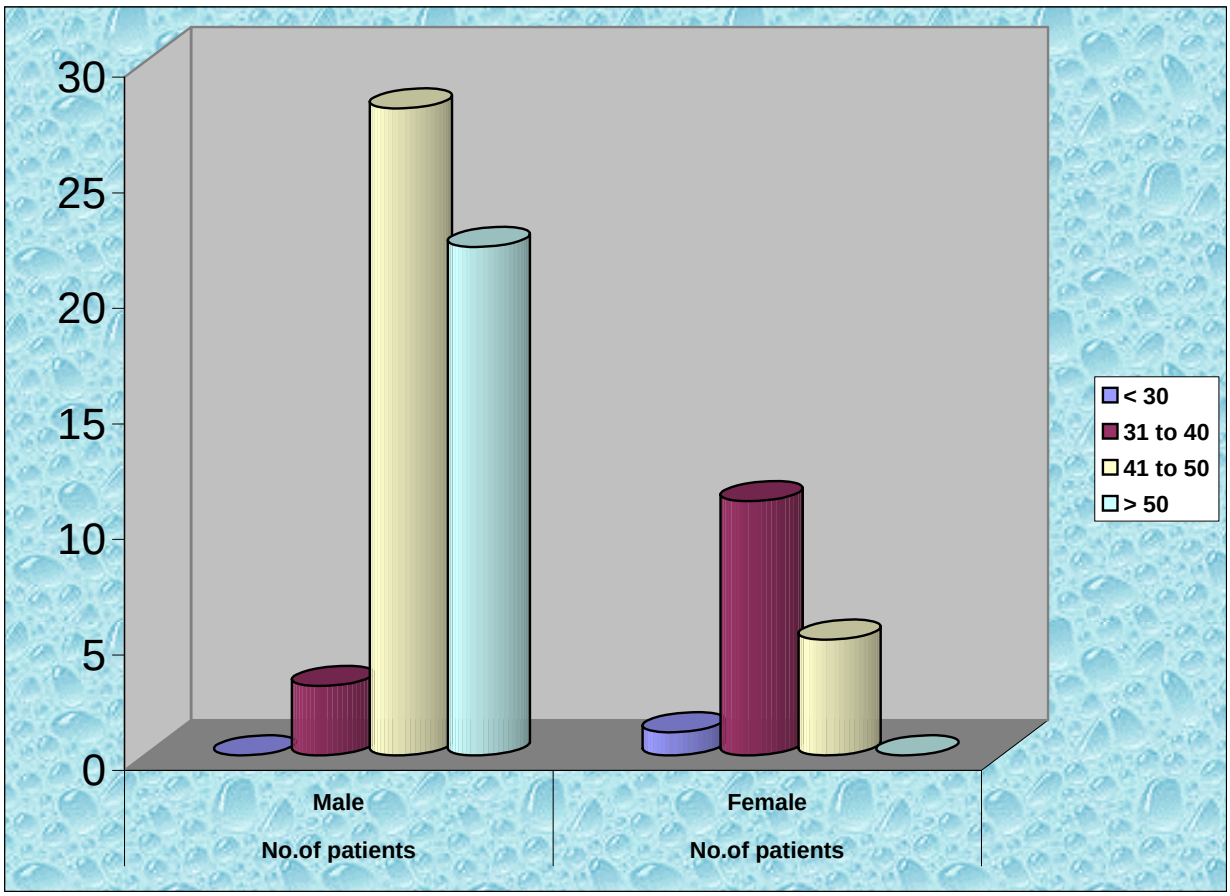


WEIGHT DISTRIBUTION

The Weight distribution was given in the following table.

Table – 3

Weight in Kg.	No.of patients Male	No.of patients Female
≤ 30	0	1
31 to 40	3	11
41 to 50	28	5
> 50	22	0

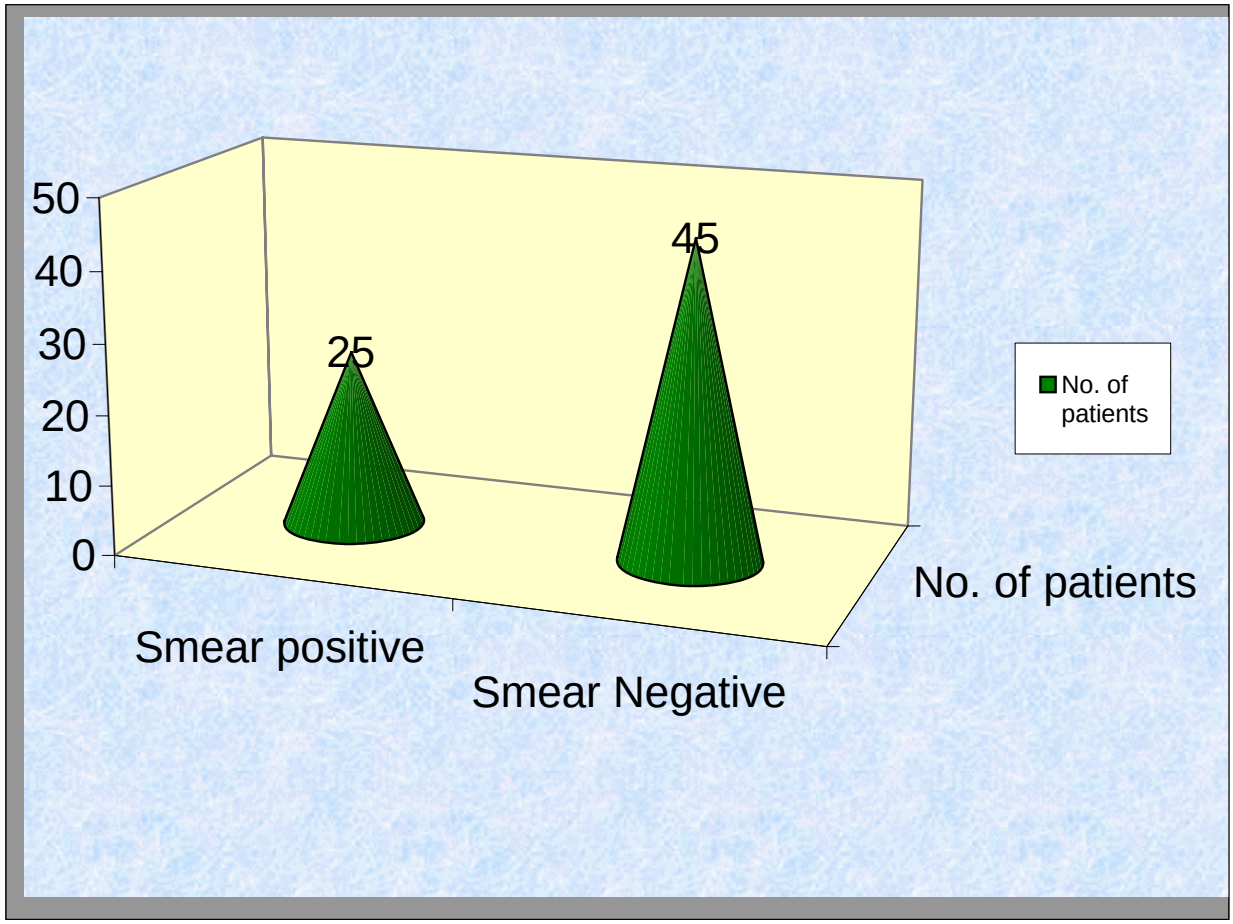


SPUTUM AFB

Sputum smear status was as follows

Table – 4

Sputum Smear Status	No. of patients
Smear positive	25
Smear Negative	45



RADIOLOGICAL PATTERNS

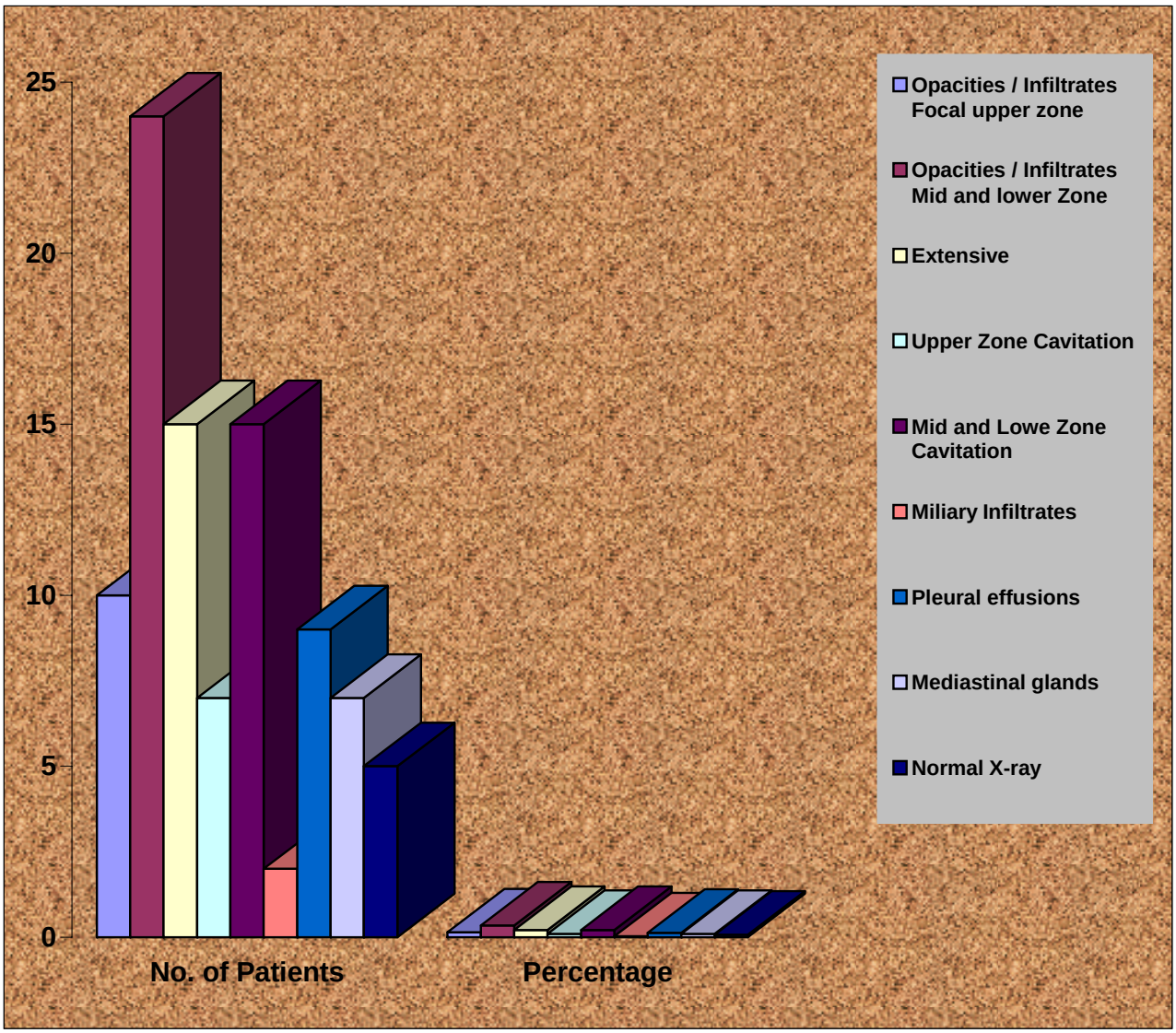
The radiological patterns were as in the following table.*

Table – 5

X-ray lesions	No. of Patients	Percentage
Opacities / Infiltrates Focal upper zone	**10**	**14.28%**
Opacities / Infiltrates Mid and lower Zone	**24**	**34.28%**
Extensive Infiltrates	**15**	**21.42 %**
Upper Zone Cavitations	**7**	**10%**
Mid and Lowe Zone Cavitations	**15**	**21.42%**
Miliary Infiltrates	**2**	**2.85%**
Pleural effusions	**9**	**12.85%**
Mediastinal glands	**7**	**10%**
Normal X-ray	**5**	**7.14%**

*- 30 patients had more than one lesion.

RADIOLOGICAL PATTERNS

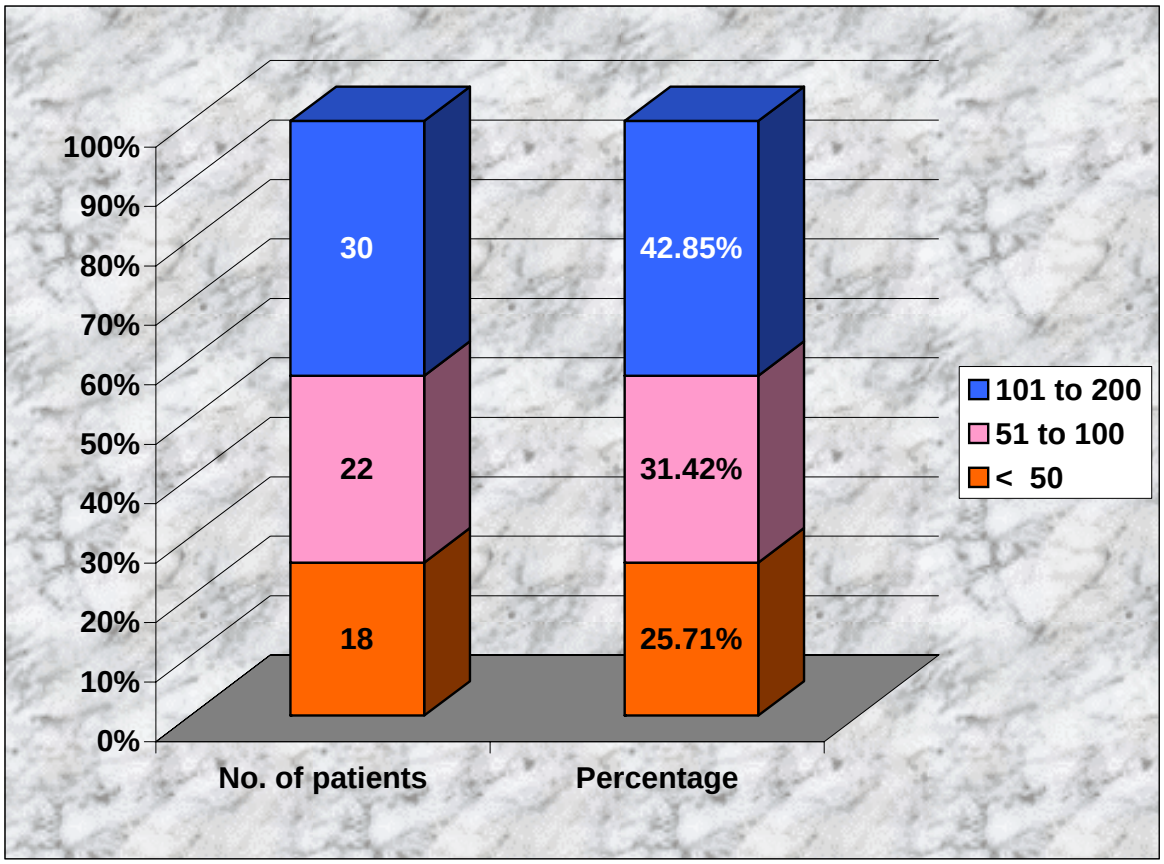


$CD4^+$ CELLS COUNT

$CD4^+$ cells count distribution was as shown in the following table.

Table - 6

$CD4^+$ cells counts per mm^3	No. of patients	Percentage
≤ 50	18	25.71 %
51 to 100	22	31.42 %
101 to 200	30	42.85 %

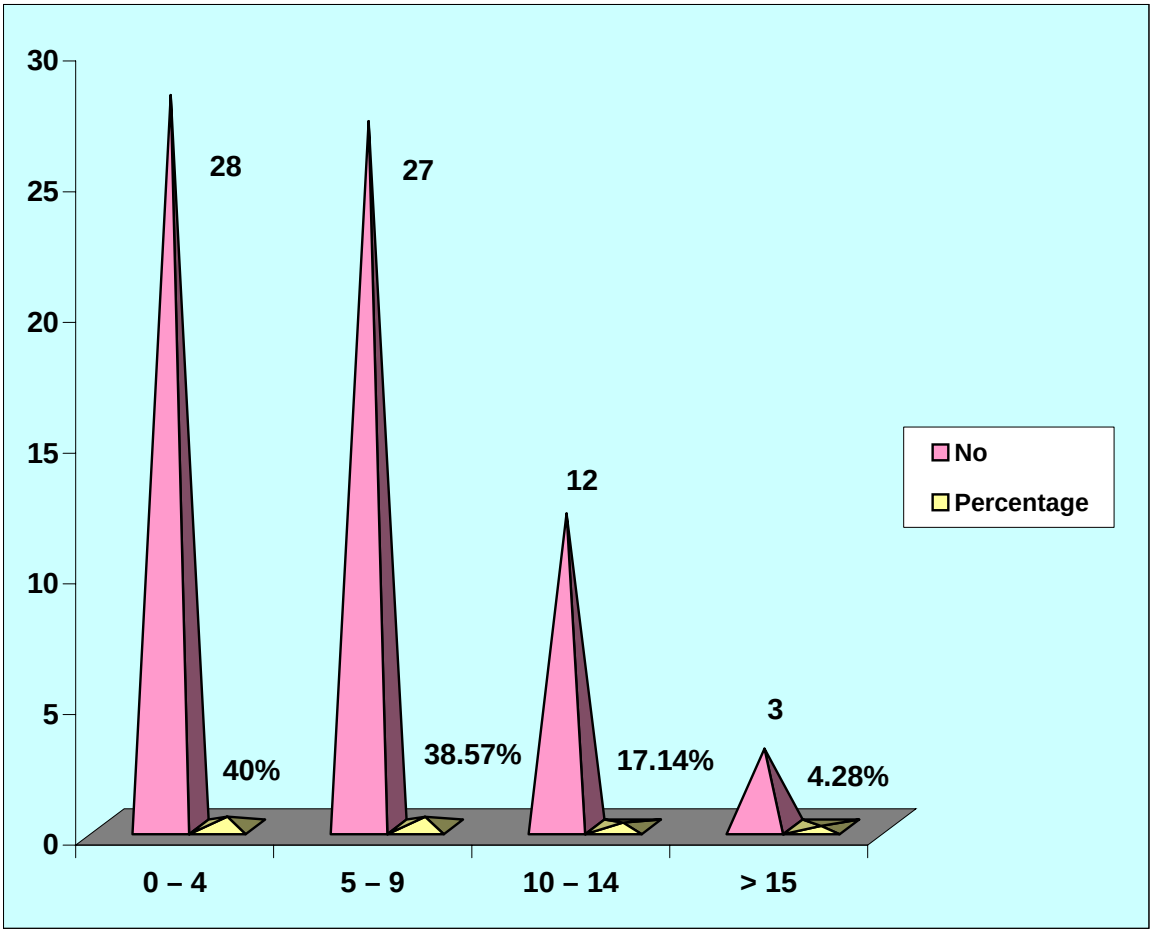


TUBERCULIN INDURATION

The distribution was as follows :

Table – 7

Tuberculin induration (mm)	No	Percentage
0 – 4	28	40%
5 – 9	27	38.57%
10 – 14	12	17.14%
≥ 15	3	4.28%

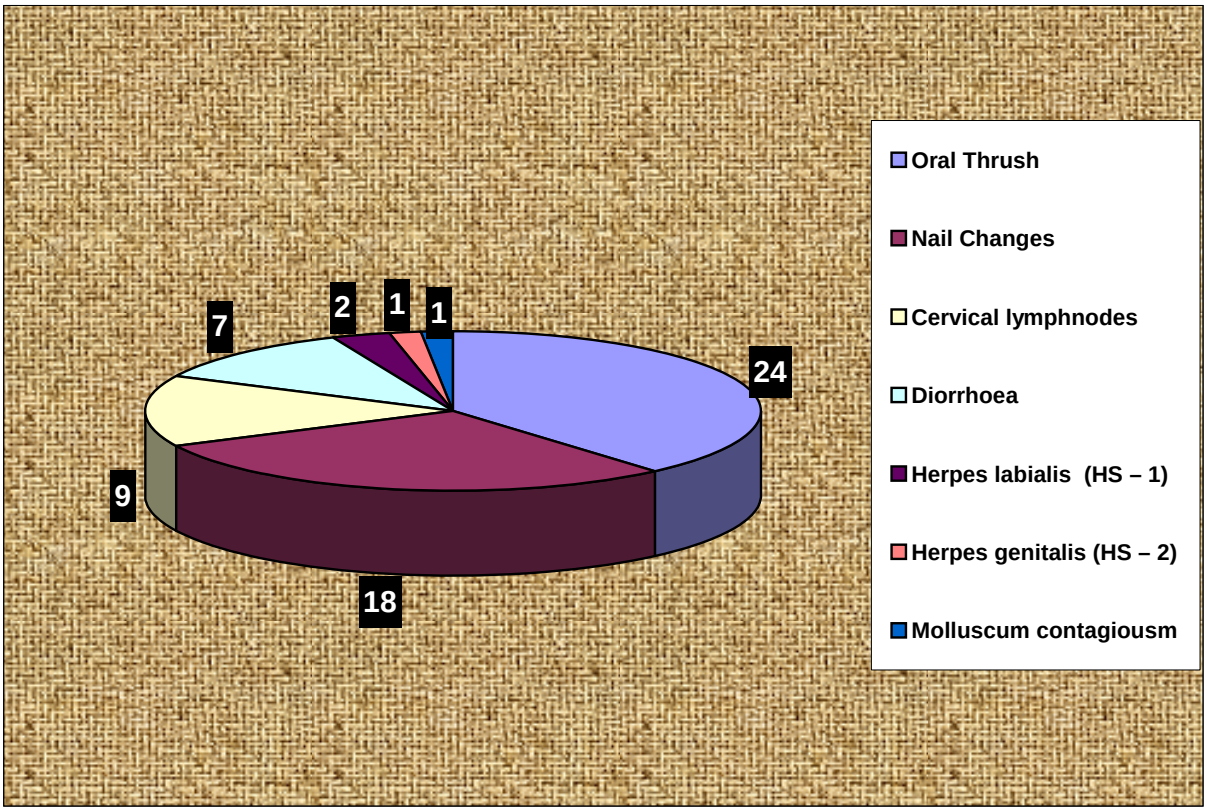


ASSOCIATED CLINICAL FEATURES

They are given as follows :

Table - 6

Clinical Features	No. of patients
Oral Thrush	24
Nail Changes	18
Cervical lymphnodes	9
Diorrhoea	7
Herpes labialis (HS – 1)	2
Herpes genitalis (HS – 2)	1
Molluscum contagiousm	1



DISCUSSION

TB is the commonest opportunistic infection in HIV positive persons in India and can develop at any stage of the HIV disease.

Here we have studied the clinical and laboratory profile of TB in advanced stages of HIV disease. ($CD4^+$ cells $\leq$ 200 cells per mm^3)

AGE DISTRIBUTION

The distribution of age group in the present study is $\leq$ 20 – 1 (about 1%), 21 to 40 – 48 (about 70%), 41 to 60 – 21 patients (30%). In Tamabram study[2], age group distribution was $\leq$ 20 – 3.19%, 21 to 40 – 74.9% and 41to 60 (20%).

Hence the present study correlates nearly with the other studies in this respect.

CLINICAL FEATURES

Of the 70 patients, most of the patients (> 90%) with clinical features of cough with expectoration, fever, weight loss and dyspnoea. In a study by Modilevsky et al[50], the frequency of clinical symptoms were cough 84%, dyspnoea 64%, diorrheoa 54% and Chest pain 25% respectively.

In a study by Soumya Swaminathan et al[3], the frequency of symptoms were cough 97%, weight loss 94%, fever 79%, dyspnoea 68%, chest pain 47% and hemoptysis 18% respectively.

In our present study the distribution were cough 91% (64), fever 91% (64), dyspnoea 94% (66), hemoptysis 19% (13) and weight loss 95% (67).

The differences may be attributed to study group variation.

Oral thrush is found to be about 35% in our study. In a study by Soumya Swaminathan et al[3], it was found to be 40% indicating the later stages of HIV disease.

The mean duration of symptoms in our study is about 2 to 3 months. In the same study mentioned above[3] the mean duration was 12 weeks.

This indicates that there was a delay in the diagnosis and treatment of Tuberculosis.

This delay may be at the patient level or at the health provider level.

EXTRAPULMONARY MANIFESTATIONS

About 26% of patients had associated extrapulmonary manifestations (i.e pleural effusion, mediastional glands). This in comparison with a study by Soumya Swaminathan et al[3], which showed that it was about 30%. Also various western studies like Jones et al[49], Shafer et al[78], revealing the range of 25 to 60%.

SPUTUM SMEAR POSITIVITY

Smear positivity in present study is about 35% (25 of 70).

In a study by Deivanayagam et al[2], it was 15%. In a study by Kleen et al[71], it was found to be 29%. The increase in number of sputum samples will tend to increase the yield of smear positivity. In patients who were sputum smear negative, the diagnosis was made by assessing the clinico – radiological spectrum.

RADIOLOGICAL PATTERNS

The radiological patterns were both typical and atypical presentation of pulmonary tuberculosis.

But atypical presentations such as lower zone infiltrates and cavities, diffuse exudative infiltrates, pleural effusions and hilar / paratracheal adenopathy were more commonly observed.

INFILTRATES

In a study by Soumya Swaminathan et al[3], the frequency were focal upper zone infiltrates – 9%, focal mid and lower zone infiltrates - 14% and extensive infiltrates - 38% respectively.

In Tambaram study[2] they were found to 34.8%, 41.5% for upper zone and mid, lower zone infiltrates.

In our study the distribution was focal upper zone infiltrates – 10 patients (nearly 15%).

Focal lower and mid zone infiltrates – 24 patients (about 35%).

Extensive infiltrates – 15 patients (about 21%).

These differences may be attributable to the advanced stages of HIV disease in whom we had studied and also difference in the study group.

CAVITARY LESION

In our study focal upper zone cavity – 7 patients (10%) and mid / lower zone cavities – 15 patients (about 21%). In Tambaram study[2] it was 17.2% and 7.6% respectively. In Soumya Swaminathan et al[3], the distribution was 11% and 3% respectively.

PLEURAL EFFUSIONS

In a study by Jones et al[49], it was 10%, in Tambaram study[2] it was 6.88% and in a study by Soumya Swaminathan et al[3] it was 12%. In the present study the frequency of pleural effusions was about 14% (9 patients).

NORMAL X-RAY

Here it was found to be in 5 patients (nearly 7 %). In western studies such as Greenberg et al[52], Long R et al[56], it was found to be present in 7 to 14% of study group and 9% of patients in the study by Soumya Sowinathan et al[3].

This may be due to the diminished immune status in which there is a decreased or no inflammatory reaction occurring in the lung parenchyma.

MILIARY TUBERCULOSIS

In our study it was present in 2 patients (3%), in a study by Batungwanoyo et al[61] it was 14% where as it was 5% and 17% in Tambaram study[2] and in a study by Soumya Swaminathan et al[3] respectively. This variation may also attributable to the difference in the study group.

MEDIASTINAL ADENOPATHY

The frequency of mediastinal adenopathy in studies by Jones et al[49] was 30% and in Batungwanoyo et al[61] it was 11% and in Soumya Swaminathan et al[3] study it was 3% where as in our study it was present in 7 patients (10%)

$CD4^+$ CELL COUNT RANGE

The range of $CD4^+$ cell count in our patients were $\leq$ 50 – 18 patients (nearly 28%), 51 to 100 – 22 patients (nearly 31%) and 101 to 200 – 30 patients (nearly 41%)

In Soumya Swaminathan et al[3] the mean $CD4^+$ cell count was 192 cells per mm^3 at base line.

TUBERCULIN TEST

The distribution of indurations were 0 to 4mm – 28 patients (40%) 5 to 9mm – 27 patients (38.57%), 10 to 14mm – 12 patients (17.14%), and more than or equal to 15mm – 3 patients (4.28%).

In Tambaram Study[2] the distribution were 0 to 4 – 33.38%, 5 to 9 – 18.62%, 10 to 14 – 22.06% and $\geq$ 15 – nearly 26%.

In study by Soumya Swaminathan et al[3], the distribution were 0 to 5mm - 56%, 6 to 10mm –3% and 11 to 20mm – 28% respectively.

This variation may be attributable to the difference in the study group population.

CONCLUSION

a) In our part of the world Tuberculosis is the common opportunistic infection even in advanced stages of HIV infection.

b) It commonly affects male in the productive age groups (21 to 40).

c) Most of the patients in advanced stages usually present with more than 3 of the 5 clinical features such as cough with expectoration, dyspnoea, fever, weight loss and hemoptysis.

d) Oral thrush is present in about 35% patients which serves as an indicator of severity of disease (HIV infection) .

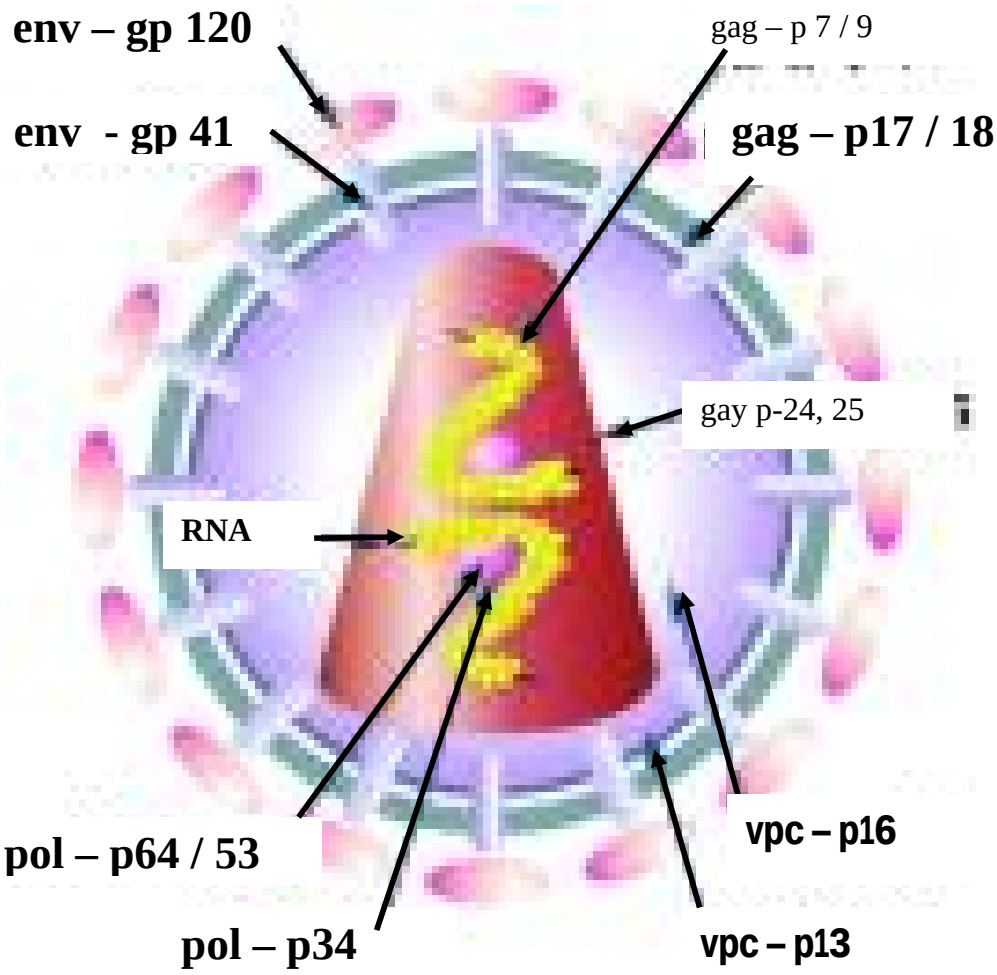
e) Patients with Tuberculosis in HIV positive persons can present with normal X-ray even in advanced stages of HIV disease also. Hence presence of normal X-ray does not rule out the possibility of Tuberculosis in HIV patients.

f) Patients in later stages of HIV infection usually present with atypical radiological patterns such as lower zone infiltrates, mid zone and lower zone cavities, pleural effusions, and hilar / paratracheal lymphadenopathy

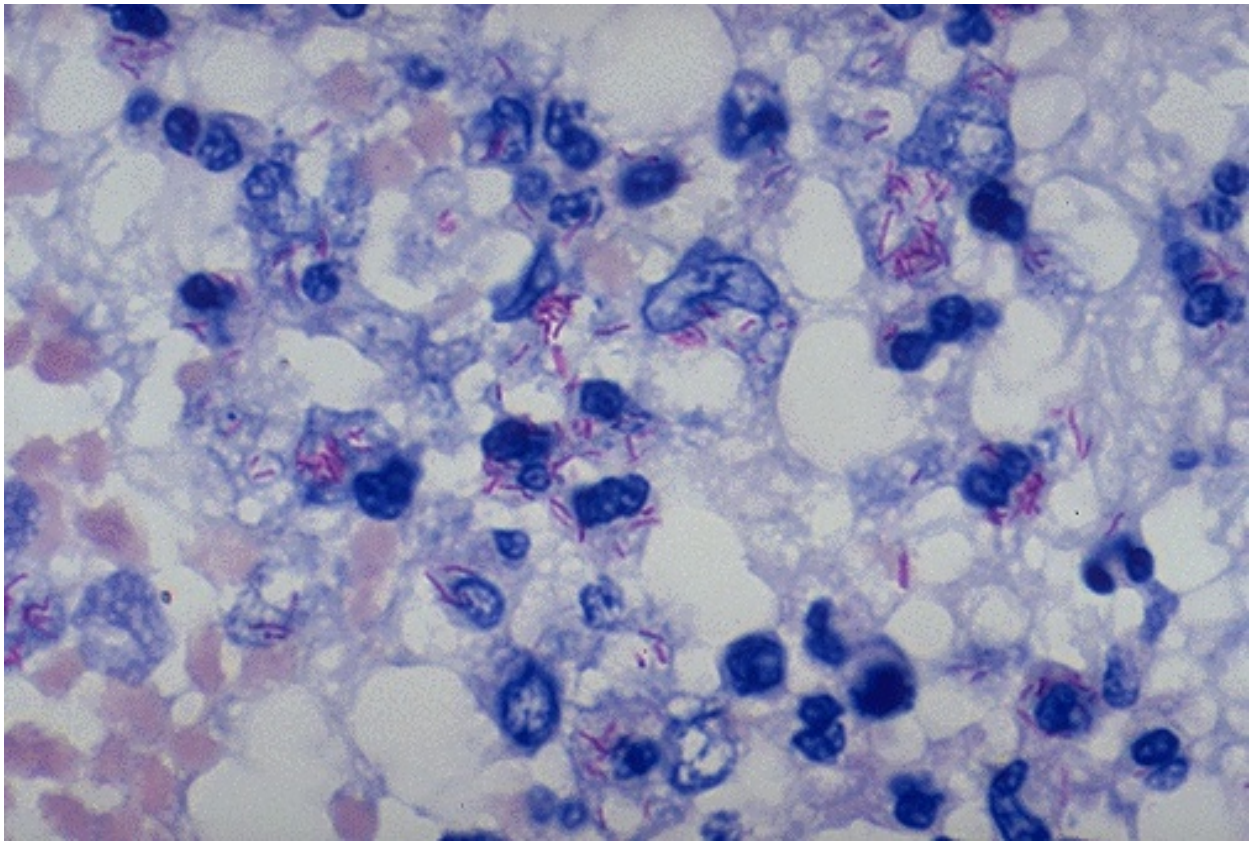
although classical upper zone infiltrates and cavities occur in less than 25 to 30% of patients.

g) Majority of the patients (42%) were in the $CD4^+$ cell counts range of 100 to 200 Cells / mm^3.

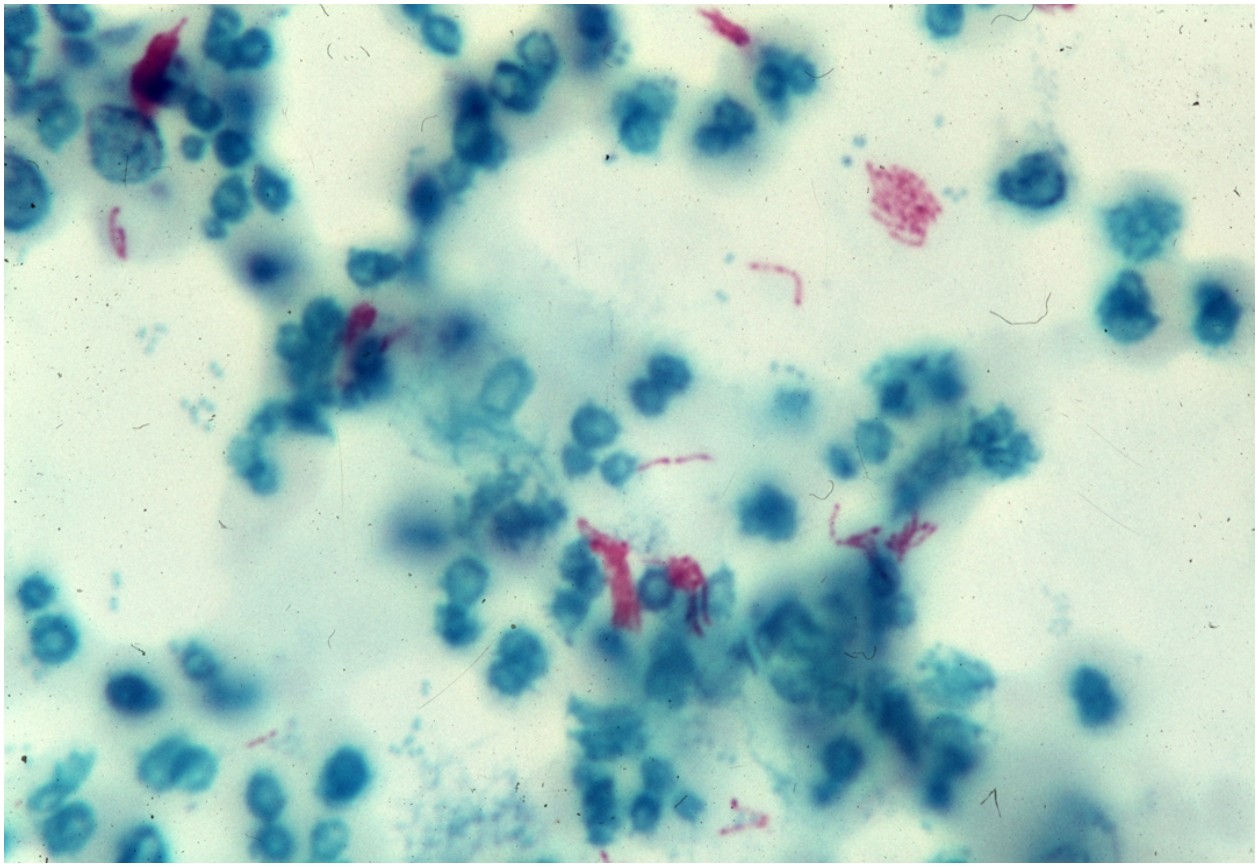
With the conventional sputum positivity and if Tuberculin test not providing an adequate diagnostic help, familiarity with the clinico – radiological spectrum of Tuberculosis is absolutely necessary.



STRUCTURE OF HIV VIRION

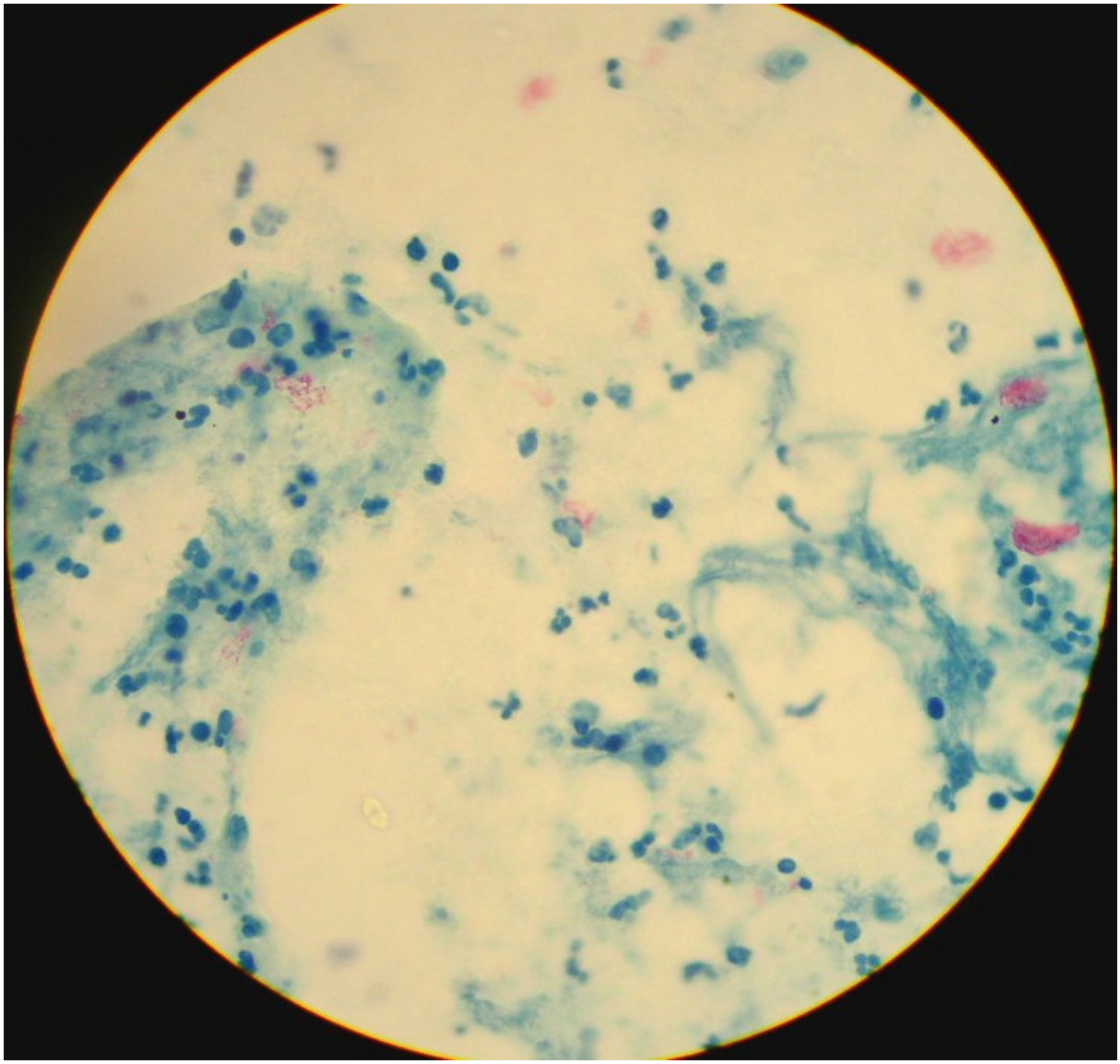


MYCOBACTERIUM TUBERCULOSIS IN CUT SECTION OF THE LUNG



ACID FAST BACILLI IN SPUTUM

(M.TUBERCULOSIS)



ACID FAST BACILLI IN SPUTUM
(M.TUBERCULOSIS)

① Airborne *Mycobacterium tuberculosis* bacteria are inhaled and lodge in the lungs

② The bacteria are phagocytized by lung macrophages and multiply within them, protected by lipid-containing cell walls

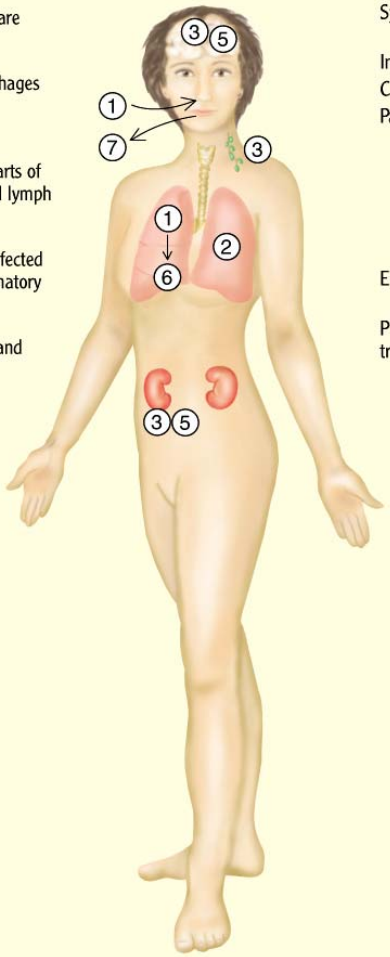
③ Infected macrophages are carried to various parts of the body such as the kidneys, brain, lungs, and lymph nodes; release of *M. tuberculosis* occurs

④ Delayed hypersensitivity develops; wherever infected *M. tuberculosis* has lodged, an intense inflammatory reaction develops

⑤ The bacteria are surrounded by macrophages and lymphocytes; growth of the bacteria ceases

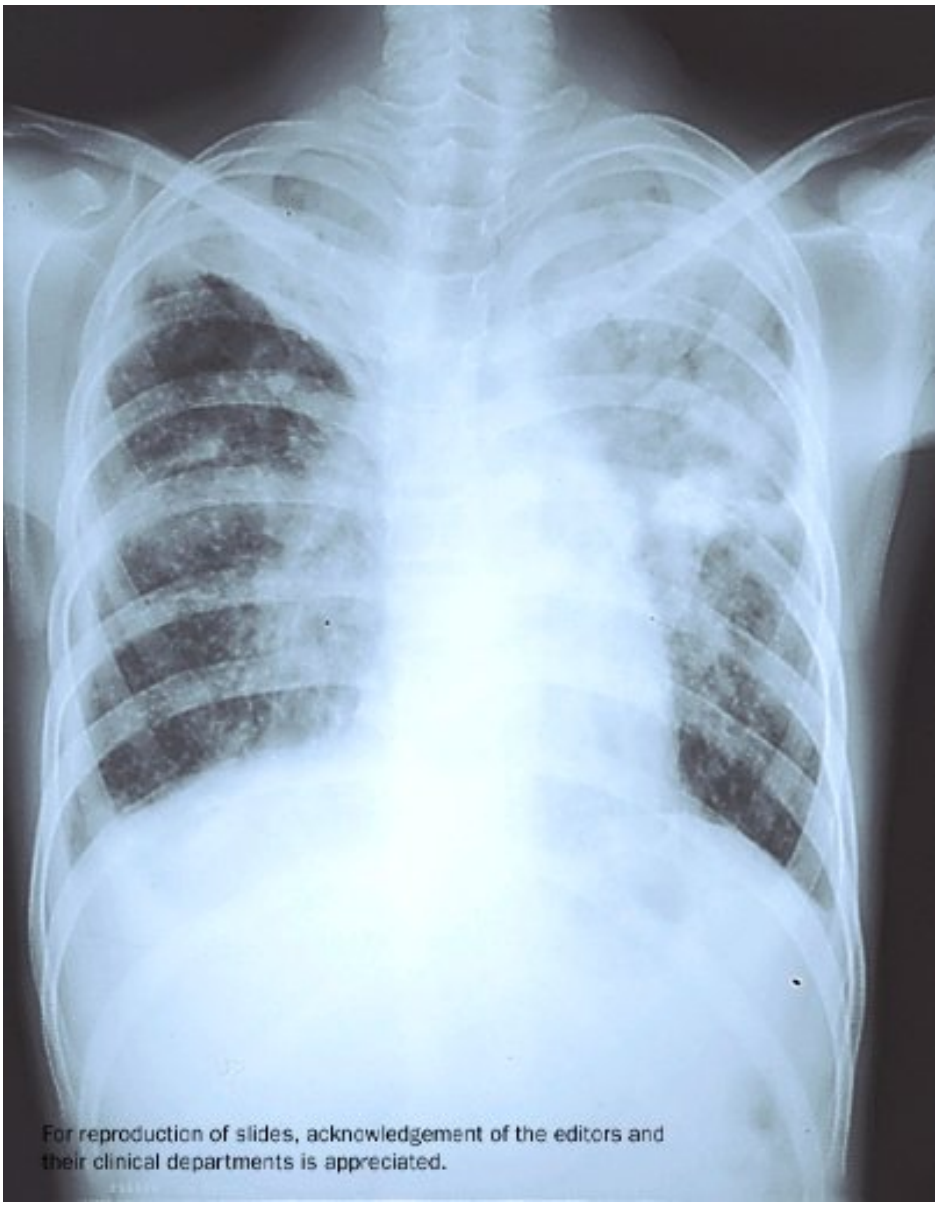
⑥ Intense inflammatory reaction and release of enzymes can cause caseation necrosis and cavity formation

⑦ With uncontrolled or reactive infection, *M. tuberculosis* exits the body through the mouth with coughing or singing



Symptoms	Fever, weight loss, cough, sputum production
Incubation period	2 to 10 weeks
Causative agent	*Mycobacterium tuberculosis*
Pathogenesis	Colonization of the alveoli incites inflammatory response; ingestion by macrophages follows; organisms survive ingestion and are carried to lymph nodes, lungs, and other body tissues; tubercle bacilli multiply; granulomas form
Epidemiology	Inhalation of airborne organisms; latent infections can reactivate
Prevention and treatment	BCG vaccination, not used in the United States; tuberculin (Mantoux) test for detection of infection, allows early therapy of cases; treatment of young people with positive tests and individuals whose skin test converts from negative to positive. Treatment: two or more antitubercular medications given simultaneously, such as isoniazid (INH) and rifampin

MYCOBACTERIUM TUBERCULOSIS IN HUMAN



X-RAY CHEST PA VIEW – PULMONARY TUBERCULOSIS

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EMC	-	Extra Maritial
PMC	-	Pre Maritial
EPI	-	Episodes
G	-	Grade
OC	-	Oral Candidias
TV	-	Tenia Versicolor
NC	-	Nail Changes (Base pigmentatio, Ridges)
D	-	Diorrhoea
MPK	-	Maculo Papular Skin Lesion
J	-	Jaundice
AG	-	Atrophic Glossitis
CRLN, CL	-	Cervical Lymphadenopathy
PE	-	Pedal Edema
KE	-	Kneejoint Effusion
GNLN, GL	-	Generalised Lymphadenopathy
HG	-	Herpes Genitalis

LT	-	Left
B	-	Bilateral
UZ - I	-	Upper Zone Infiltrates
LZ - I	-	Lower / Mid Zone Infiltrates
UZ - C	-	Upper Zone Cavity
LZ - C	-	Lower / Mid Zone Cavity
ML - I	-	Miliary Infiltrates
PE	-	Pleural Effusions
HSL	-	Herpes Labialis
PRL	-	Paratracheal Lymphadenopathy
PAL	-	Para Aortic Lymphadenopathy
RPL	-	Retro Peritoneal Lymphadenopathy
HL	-	Hilar Adenopathy
EXT - I	-	Extensive Infiltrates
RT	-	Right
(I)	-	In patients
WNL	-	Within normal limit